Informalities

The Office Action states that, on page 1, line 1 of the specification, the priority/continuing data is missing. Upon entry of the above amendments, Applicants have amended the first paragraph of the specification to recite the priority data.

The Office Action states that amended claim 1 is objected to because it repeats line 2 at page 1 in line 1 at page 2. Accordingly, upon entry of the above amendments, Applicants have amended claim 1 to remove the duplicate line.

Priority

The Office Action states that the application fails to provide a certified copy of the English translation in support of the priority date claimed. In response, Applicants respectfully submit herewith a verified English translation of the priority document.

Information Disclosure Statement

The Office Action states that reference D on the PTO-1449 form filed on April 24, 2001 has not been considered because an English translation of reference D has not been submitted. Applicants respectfully note that the abstract of reference D is in English, as are the graphs and tables. In addition to these disclosures in English, Applicants respectfully submit herewith an English translation of the relevant portion of reference D.

Objections to Claims

The Office Action states that claims 4, 5, 9 and 10 are objected to under 37 CFR § 1.75(c) as being in improper form because a multiple dependent claim cannot depend from any other multiple dependent claim. Accordingly, Applicants have amended claim 3 to be dependent only on claim 1 and claim 8 to be dependent only on claim 6. As such, Applicants respectfully request that the claim objections be removed.

Claim Rejections

35 U.S.C. § 112, Second Paragraph

The Office Action states that claims 4-5 and 9-10 are rejected as being indefinite because they are multiple dependent claims from previous multiple dependent claims 3-4 and 8-9, respectively. Accordingly, Applicants have amended claim 3 to be dependent only on claim 1 and claim 8 to be dependent only on claim 6. As such, Applicants respectfully

claim 1 and claim 8 to be dependent only on claim 6. As such, Applicants respectfully request that the claim rejections be removed.

The Office Action states that claims 1-10 are indefinite because of the use of the term "cGMP". Applicants have amended claims 1 and 6 to recite "cyclic guanosine 3',5'-monophosphate (cGMP)". Accordingly, Applicants respectfully request that these rejections be removed.

The Office Action states that claims 6-10 are indefinite because they lack essential steps as claimed in the process of treatment or prophylaxis of ischemic heart diseases. Accordingly, Applicants have amended claim 6 to recite that the active ingredient is administered "before the initiation of, during and/or following to ischemia reperfusion therapy." Further, Applicants respectfully submit that the nature of "a method of treatment" differs from that of "a process" wherein the steps are considered to be the essential features. In the method of treatment of the present application, administration routes, methods of administration and the dose range of the active ingredient are described in the specification, and can be appropriately determined by a doctor depending on a patient to be treated, and a ordinarily skilled person will easily understand the invention by reading claim 6. For at least the foregoing reasons, Applicants respectfully request that these rejections be removed.

35 U.S.C. § 102(b)

The Office Action states that claims 1-10 are rejected under 35 U.S.C. § 102(b) as being anticipated by Takata et al. (Cardiovascular Research, 32, 286-293, 1996). In particular, the Office Action states that Takata et al. teach a pharmaceutical composition that comprises an effective amount of synthetic alpha human ANP, which increases the level of cGMP, and has cardioprotective effects on myocardial ischemia and reperfusion injury. However, Applicants respectfully submit that the myocardioprotective effect of ANP disclosed by Takata et al. is simply the suppression of arrhythmia such as ventricular extrasystoles or the suppression of the decrease of intra-cellular high-energy phosphates. In contrast, the present invention comprises reducing an infarct region resulting from the ischemic necrosis. For example, at page 3, lines 19-23, the specification recites that, "The inventors of the present invention further studied the properties of natriuretic peptides, and found for the first time that these peptides can reduce an infarct region occurring in a model of acute myocardial infarction involving ischemia reperfusion." Accordingly, Applicants respectfully submit that the present claims are distinguished from Takata et al. as Takata et al.

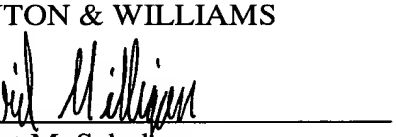
For at least the foregoing reasons, Applicants respectfully request that the rejections under 35 U.S.C. § 102(b) be removed.

Conclusion

Applicants believe that incorporation of the above amendments, further in view of the above remarks, have placed this application in a condition for allowance. Early notification of a favorable consideration is respectfully requested. In the event that the Examiner has any questions concerning this Response, or the above-identified application in general, the Examiner is invited to contact the undersigned attorney concerning such questions so that prosecution of this application may be expedited. Should any fees be due in connection with the filing of this Amendment, the Commissioner is authorized to charge them to Deposit Account No. 50-0206.

Respectfully submitted,

HUNTON & WILLIAMS

Date: December 10, 2002 By: 

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ATTACHMENT A

Version With Markings To Show Changes Made to Specification

Please replace the first paragraph of the specification, page 1, lines 4-9, with the following replacement paragraph:

--This applications claims priority of Japanese Application No. 98134/2000, filed on March 31, 2000. This invention relates to a pharmaceutical composition for reducing an infarct region resulting from the ischemic necrosis of cells, the pharmaceutical composition containing a substance, as an active ingredient, which can increase intracellular cGMP production by acting on a natriuretic peptide receptor.--

Please replace the second paragraph on page 9, lines 7-16, with the following replacement paragraph:

--The dose of the pharmaceutical composition of the present invention differs according to the age, the body weight, the severity of symptoms of, and the route of administration in, a patient with myocardial infarction or a patient potentially developing myocardial infarction. When the substance as an active ingredient is a natriuretic peptide, the pharmaceutical composition can be administered at a dose of 0.1 μg/kg/min to 0.2 μg/kg/min, and is preferably administered in a dose of 0.025 μg/kg/min to 0.1 μg/kg/min, by the continuous intravenous route. When the administration is made by coronary infusion, a higher dose of the active ingredient can be administered than in the case of an intravenous administration.--

ATTACHMENT B

Version With Markings To Show Changes Made to Claims

--1. (Twice Amended) A pharmaceutical composition for use in treatment or prophylaxis of [ischemic heart disease, the pharmaceutical composition comprising a substance, as an active] ischemic heart disease, the pharmaceutical composition comprising a substance, as an active ingredient, which can increase intracellular cyclic guanosine 3',5'-monophosphate (cGMP) production by acting on a natriuretic peptide receptor, and which has an effect of reducing an infarct region.--

--3. (Amended) The pharmaceutical composition of claim 1 [or 2], wherein the ischemic heart disease is myocardial infarction.--

--6. (Amended) A method of treatment or prophylaxis of ischemic heart disease, comprising administering to a patient who is in need of such a treatment or prophylaxis a substance, as an active ingredient, which can increase intracellular cyclic guanosine 3',5'-monophosphate (cGMP) production by acting on a natriuretic peptide receptor, and which has an effect of reducing an infarct region, before the initiation of, during and/or following to ischemia reperfusion therapy.--

--8. (Amended) The method of claim 6 [or 7], wherein the ischemic heart disease is myocardial infarction.--

--11. (Added) A method for reducing an infarct region or suppressing enlargement of an infarct region in the heart of a patient who is suffering from or has a potential risk of suffering from infarct resulting from ischemic necrosis as an ischemia reperfusion injury, wherein said method comprises:

administering a substance capable of acting on a natriuretic peptide receptor to increase the production of cellular cyclic guanosine 3',5'-monophosphate (cGMP), at an amount effective for reducing the infarct region or suppressing enlargement of an infarct

region to said patient before the initiation of, during and/or following ischemia reperfusion.--

--12. (Added) A method of claim 11, wherein the active ingredient is a natriuretic peptide selected from the group consisting of atrial natriuretic peptide (ANP), brain natriuretic peptide (BNP) and C-type natriuretic peptide (CNP).--

--13. (Added) A method of claim 12, wherein the active ingredient is administered at a dose between 0.01 μg/kg/ml and 0.2 μg/kg/ml by continuous infusion.--

--14. (Added) A method of claim 13, wherein the active ingredient is administered at a dose between 0.025 μg/kg/ml and 0.1 μg/kg/ml.--

--15. (Added) A method of any one of claims 12, 13 and 14, wherein the infusion is made by an intravenous injection.--

--16. (Added) A method by any one of claims 12, 13 and 14, wherein the infusion is made by a coronary injection.--